03/21/2008

UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Rey 1459

P O Box 1450 Alexandria, Virgima 22313-1450

### NOTICE OF ALLOWANCE AND FEE(S) DUE

36335 7590
GE HEALTHCARE, INC.
IP DEPARTMENT
101 CARNEGIE CENTER
PRINCETON, NJ 08540-6231

EXAMINER
AUDET, MAURY A

ART UNIT PAPER NUMBER

1654

DATE MAILED: 03/21/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,487	01/30/2006	Alan Cuthbertson	PN0360	3640
TITLE OF INVENTION: IT	MAGING AGENTS			

APPLN, TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1440	\$300	\$0	\$1740	06/23/2008

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 1SI. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

#### HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and I/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

#### PART B - FEE(S) TRANSMITTAL

# Complete and send this form, together with applicable fee(s), to: Mail Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

or Fax (571)-273-2885

appropriate. All further indicated unless corrects maintenance fee notifica	correspondence includired below or directed oth	ng the Patent, advance onerwise in Block 1, by (	rders and notification of r a) specifying a new corre	naintenance fees wi spondence address;	ill be and/or	mailed to the current (b) indicating a sepa	correspondence address as rate "FEE ADDRESS" for
		iock 1 for any change of address)	pap	ers. Each additional	paper	can only be used for icate cannot be used for such as an assignment ling or transmission.	domestic mailings of the or any other accompanying at or formal drawing, must
36335 GE HEALTHO IP DEPARTME 101 CARNEGIE	NT E CENTER	/2008	I be	Cert	ificate	of Mailing or Trans	nission deposited with the United t class mail in an envelope above, or being facsimile tte indicated below.
PRINCETON, N	U 08540-6231						(Depositor's name)
			<u> </u>				(Signature)
							(Date)
APPLICATION NO.	FILING DATE		FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.		CONFIRMATION NO.
10/566,487 TITLE OF INVENTION	01/30/2006 : IMAGING AGENTS		Alan Cuthbertson			PN0360	3640
APPLN. TYPE	SMALL ENTITY	ISSUE PEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE	FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1440	\$300	\$0		\$1740	06/23/2008
EXAM	INER	ART UNIT	CLASS-SUBCLASS	1			
AUDET, M	AURY A	1654	514-002000	•			
"Fee Address" ind PTO/SB/47; Rev 03-0 Number is required.  3. ASSIGNEE NAME A	ondence address (or Cha 3/122) attached. ication (or "Fee Address 12 or more recent) attach ND RESIDENCE DAT/ less an assignee is ident h in 37 CFR 3.11. Comp	inge of Correspondence "Indication form and. Use of a Customer A TO BE PRINTED ON	2. For printing on the p  (1) the names of up to or agents OR, alternati (2) the name of a singl registered attorney or 2 registered patent atto listed, no name will be THE PATENT (print or ty) data will appear on the p TT a substitute for filing an GB RESIDENCE: CCTTY	3 registered patent vely, e firm (having as a agent) and the name rneys or agents. If n printed.	memb s of u so nam	er a 2o to e is 3	cument has been filed for
4a. The following fee(s)	are submitted:		b. Payment of Fee(s): (Plea	se first reapply an	y prev	lously paid issue fee	up entity Government
☐ Publication Fee (No small entity discount permitted) ☐ Advance Order - # of Copies			☐ Payment by credit card. Form PTO-2038 is attached. ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number (enclose an extra copy of this form).				
	s SMALL ENTITY state	as. See 37 CFR 1.27.	b. Applicant is no lon				
interest as shown by the	records of the United Sta	ites Patent and Trademark	Office.	ne applicant, a regis	acreu a	ittorney or agent, or th	e assignee or other party in
Authorized Signature				Date			
Typed or printed name				Registration No			
This collection of inform an application. Confiden submitting the completes this form and/or suggesti Box 1450, Alexandria, V Alexandria, Virginia 223	ation is required by 37 C tiality is governed by 35 d application form to the ions for reducing this but friginia 22313-1450. DC 13-1450.	CFR 1.311. The informatic U.S.C. 122 and 37 CFR USPTO. Time will vary rden, should be sent to the ONOT SEND FEES OR	on is required to obtain or 1.14. This collection is est depending upon the indivention of fice COMPLETED FORMS TO COMPLETED FORMS TO TO TO T	retain a benefit by the timated to take 12 m ridual case. Any cor er, U.S. Patent and 1 D THIS ADDRESS.	ne publ ninutes nment Fraden SENI	ic which is to file (and to complete, includin s on the amount of tir nark Office, U.S. Depa D TO: Commissioner I	by the USPTO to process) g gathering, preparing, and ne you require to complete rtment of Commerce, P.O. or Patents, P.O. Box 1450,

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.



# UNITED STATES PATENT AND TRADEMARK OFFICE

#### UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS

P O Box 1450 Alexandria, Virgima 22313-1450 www.uspto.gov

APPLICATION N	О.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.	
10/566,487		01/30/2006	Alan Cuthbertson	PN0360	3640	
36335	7590	03/21/2008		EXAMINER		
GE HEALTHCARE, INC.			AUDET, M	MAURY A		
IP DEPART!				ART UNIT	PAPER NUMBER	
101 CARNE PRINCETON				1654 DATE MAII ED: 03/21/200	8	

# Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

# Notice of Allowability

Application No.	Applicant(s)	
10/566,487	CUTHBERTSON ET AL.	
Examiner	Art Unit	
MALIRY ALIDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address-All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included
herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. THIS
NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative
of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

- This communication is responsive to the response of 10/24/07.
- 2. The allowed claim(s) is/are 1-8 and 10-14.
- 3. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) 

    All b) 

    Some\* c) 

    None of the:
    - 1. A Certified copies of the priority documents have been received.
    - 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_
      - Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
  - \* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

- 4. A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
- 5. CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1) 🔲 hereto or 2) 🔲 to Paper No./Mail Date \_\_\_\_\_
  - (b) including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

 DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

## Attachment(s)

- 1. Notice of References Cited (PTO-892)
- 2. Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3. Information Disclosure Statements (PTO/SB/08),
- Paper No./Mail Date \_\_\_\_\_\_

  4. Examiner's Comment Regarding Requirement for Deposit of Biological Material
- 5. Notice of Informal Patent Application
- Interview Summary (PTO-413), Paper No./Mail Date .
- 7. 

  Examiner's Amendment/Comment
- 8. X Examiner's Statement of Reasons for Allowance
- 9. Other \_\_\_\_\_.

/Cecilia Tsang/ Supervisory Patent Examiner Art Unit 1654 Application/Control Number: 10/566,487 Page 2

Art Unit: 1654

# REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: the presently claimed bicyclic peptides compounds of formula (I) were not found to be reasonably taught or suggested in an updated search of the prior art of record.

The findings of the International Authority in the search report of related PCT/GB2004/003150, as noted in the previous action, are also noted (citing seven "A" references):

# Novelty and Inventive Step (Article 33(2)(3) PCT)

The present application addresses bicyclic peptides having the amino acid sequence KCRGDCFC being substituted at the C-terminus with a PEGylated moiety, at the 6-amino group with an antineoplastic agent, a chelating agent or a reporter group bound via a linker molecule of the PEG-type. The C-terminal cysteine sulfur is bound as thioether via a methylene carbonyl group to the N-terminus. The other cysteines are bridged via a S-(CH2)1.4-S link. These compounds are also claimed as being used in radiopharmaceutical compositions, a method for in vivo diagnosis. A method of preparation is claimed too.

D1, which considered representing the closest prior art, discloses compounds which differ only in the lack of the methylene groups between the sulfur atoms of the Cys-Cys bridge. The other prior art documents are more remote concerning the amino acid sequence as well as the nature of the bridges forming the cyclic peptides. The subject-matter of present claims 1-14 is therefore novel.

Taking the disclosure of D1 into consideration, the problem underlying the present application is to be regarded as to provide further alternative bicyclic peptides which can act as targeting compounds in diagnosis and therapy of diseases related to VEGF, i.e. to neovascularisation, thereby being chemically robust against attacks to the bicyclic structure which stabilizes the particular conformation (see also pages 5 to 6 of D1). The solution presented by the present application is the introduction of a methylene group linking the Cys sulfurs. This solution is not suggested by the closest prior art alone or in combination with any of the prior art documents D2 to D7. D3 discusses the influence of the ring size upon the activity of backbone cyclised radiolabelled somatostatin analogues but mentions explicitly that bridges involving side chains of the amino acids should be avoided in order to prevent negative effects on the ligand binding to the receptor. The teaching of this document leads the skilled person away from the proposed solution. The other documents do not even deal with the problem of the stability of conformationally constrained bicyclic peptides. The subject-matter of present claims 14 is thus considered involving an inventive step.

Art Unit: 1654

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

#### Conclusion

Claims 1-8 and 10-14 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Application/Control Number: 10/566,487 Page 4

Information regarding the status of an application may be obtained from the Patent

Art Unit: 1654

Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free), If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MA, 3/15/08

/Cecilia Tsang/

Supervisory Patent Examiner, Art Unit 1654